Supplementary data

Table 1: Number of patients enrolled by participating centre

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| --- | --- |
| **Centre** | **Number of patients** |
| SHaRE consortium | 250 (59.4%) |
| Necker –Enfants Malades hospital, Paris, France  | 63 (15%) |
| Heart muscle disease registry Trieste, | 13 (3.1%) |
| Hospital Saint Joseph, Marseille, France | 1 (0.2%) |
| Charite – Universitatsmedizin Berlin, Germany | 17 (4.0%) |
| Rio Hortega University Hospital, Valladolid, Spain | 3 (0.7%) |
| Helsinki University Hospital | 16 (3.8%) |
| Hokkaido University Hospital, Sapporo, Japan | 12 (2.9%) |
| Fondazione Toscana G Monasterio, Massa-Pisa, Italy | 12 (2.9%) |
| Children’s Hospital ‘Louis Turcanu’, Timisoara, Romania  | 4 (1.0%) |
| Great Ormond Street Hospital, London, UK  | 30 (7.1%) |

Table 2: Characteristics of predictors before and after imputation

|  |  |  |
| --- | --- | --- |
|  | **Original data** | **After imputation** |
|  | **Missing %** | **N (%) or Mean, Median (Range)** |  **No. of patients with SCD** | **N (%) or Mean, Median (Range)** |  **No. of patients with SCD** |
| **NSVT** | 41.6 | 3.3 | 1 | 5.1 | 2 |
| **LVOT** | 57.2 | 25.59;10; 2-250 | 18 | 27.96,10, 2-250 | 23 |
| **zscoreLA** | 37.3 | 1.30;1.22;-5.51-15.3 | 20 | 1.28;1.21;-5.51-15.3 | 23 |

Table 3: Proportion of patients with missing data in HCM Risk-Kids predictor variables by outcome

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| --- | --- | --- | --- |
| **HCM Risk-kids predictor variable**  | **SCD end-point (n=39)** | **No SCD end-point (n=382)** | **P value**  |
| Unexplained syncope  | 0 | 0 | >0.999 |
| NSVT  | 14 (35.9%) | 161 (42.2%) | 0.451 |
| MWT z score (n=354) | 2 (5.1%) | 11 (2.9%) | 0.439 |
| LA diameter z score (n=264) | 9 (23.1%) | 148 (38.7%) | 0.054 |
| LVOT gradient (n=205) | 8 (20.5%) | 208 (54.5%) | <0.001 |

Table 4: Clinical characteristics of patients experiencing a sudden cardiac event with an HCM Risk-Kids estimated 5-year risk of < 6%

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Age (years) | FHx | Unexplained syncope | NSVT | MLVWT (mm, Z score) | LA (mm, z score) | LVOT gradient (mmHg) | Genetics | Estimated risk of SCD | Event  |
| 2.5  | No FHx HCM/SCD | 0 | 0 | 8, +5.0 | 12, -3.3 | - | - | 1.6% | SCD aged 3.8 years |
| 4.7  | FHx of SCD | 0 | - | 11, +7.3 | 25, +1.0 | 12 | Negative extended panel (104 genes) | 3.8% | Resuscitated cardiac arrest aged 6yrs |
| 8.5  | FHx of HCM | 0 | 0 | 16, + 9.0 | 32, +1.0 | 46 | Negative panel (9 genes) | 3.8% | Resuscitated cardiac arrest aged 12.4 years |
| 12.7  | FHx of HCM | 0 | 0 | 11, +4.2 | 22, -1.7 | 7 | Negative panel (2 genes) | 1.7% | Sustained VT aged 17 years  |
| 14.3  | No FHx HCM/SCD | 0 | 0 | 22.4, + 11.6 | 32,-0.5 | 5 | -  | 5.6% | SCD aged 15.8 years  |
| 16.5  | FHx HCM and SCD | 0 | 0 | 13, + 4.8 | 40+2.2 | - | MYH7 p.Lle702Asn | 3.2% | SCD aged 19.6 years+ |

FHx = Family history, HCM = hypertrophic cardiomyopathy, SCD = sudden cardiac death, NSVT = non-sustained ventricular tachycardia, MLVWT = maximal left ventricular wall thickness, LA = left atrial, LVOT = left ventricular outflow tract

HCM Risk-Kids estimates of 5-year sudden cardiac death risk calculated from single imputed dataset. (-) indicates missing data for predictor variable

+Calculation of risk using adult model (HCM-Risk SCD) estimated risk at 5 years 3.2%

Table 5: Comparison of the effect of using different thresholds of HCM Risk-Kids estimated risk of sudden cardiac death-event for implantable cardioverter defibrillator (ICD) implantation decisions

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| --- | --- | --- | --- | --- | --- | --- | --- |
|  HCM Risk-Kids estimated 5-year risk of event  | Sensitivity  | Specificity | PPV | NPV | Events in ‘low’ risk | Events in ‘high’risk | Number of patients with an ICD without an event at 5 years  |
| $\geq $5% | 78.3% | 65.6% | 11.6% | 98.1% | 5 (21.7%) | 18(78.7%) | 137 (88.4%) |
| $\geq $6% | 73.9% | 72.9% | 13.6% | 98.0% | 6(26.1%) | 17(73.9%) | 108(86.4%) |
| $\geq $7% | 69.6% | 77.9% | 15.4% | 97.8% | 7(30.5%) | 16(69.6%) | 88 (84.6%) |
| $\geq $8% | 56.5% | 84.2% | 17.1% | 97.1% | 10 (43.5%) | 13(56.5%) | 63 (82.9%) |

Estimated from a single imputed dataset.

HCM=hypertrophic cardiomyopathy, PPV=positive predictive value, NPV=negative predictive value

Figure 1: Description of external validation cohort (VF= ventricular fibrillation, VT= ventricular tachycardia, FU=follow-up)